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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,453	06/13/2002	Song F Lee	DALHO1340-1	5725

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EXAMINER

LI, QIAN JANICE

ART UNIT PAPER NUMBER

1632

DATE MAILED: 01/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/019,453

Applicant(s)

LEE ET AL.

Examiner

Q. Janice Li

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 3, 11 and 14-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-10, 12 and 13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1, 2, 4-13, and species election drawn to a pathogen that is *Bordetella pertussis* is acknowledged. The traversal is on the ground(s) that Groups I and II, or III and IV have the same classification and could readily be searched together, and related as product and process of use. This is not found persuasive because it is maintained that each of the Inventions requires a separate search status and consideration. The inventions are mutually exclusive and independent products and methods for *in vivo* and *ex vivo* vaccines. For example, the oral organism carrying antigens from one pathogen would induce a different immune response and have a different mode of action from that carrying antigens from a plurality of different pathogens. As such, the Invention of group II is a different composition, and thus requires different search criteria and technical considerations compared to the Invention of group I. The searches for groups II and I would have certain overlap, but they are not co-extensive. In view of the amount of information in today's patent and non-patent databases, a search for all the groups would impose serious burden on the Office.

Upon further consideration, the original restriction of groups I and II has been modified as following: Group I, drawn to claims 2, 5-8; and Group II, drawn to claim 3. Claims 1, 4, 9-13 link inventions I and II. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 1, 4, 9-13. Upon

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the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

As to the product and process of using, as discussed in the previous Office action, the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the process for using the product of group I as claimed can be practiced with another and materially different product such as the product of group II. Further, a search for the invention of the product and process of use groups would not be coextensive because a search indicating the process is novel or unobvious would not extend to a holding that the product itself is novel or unobvious; similarly, a search indicating that the product is known or would have been obvious would not extend to a holding that the process is known or would have been obvious. Therefore, restriction for examination purposes as

indicated is proper. M.P.E.P. states, "FOR PURPOSES OF THE INITIAL REQUIREMENT, A SERIOUS BURDEN ON THE EXAMINER MAY BE PRIMA FACIE SHOWN IF THE EXAMINER SHOWS BY APPROPRIATE EXPLANATION OF SEPARATE CLASSIFICATION, OR SEPARATE STATUS IN THE ART, OR A DIFFERENT FIELD OF SEARCH AS DEFINED IN MPEP § 808.02". Accordingly, it is maintained that these inventions are distinct due to their divergent subject matter. Further search of these inventions is not co-extensive, as indicated by the separate classifications. The requirement is still deemed proper and is therefore made **FINAL**.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Further, as indicated in the previous Office action, the rejoinder practice applies to this application, i.e. once the product claims are subsequently found to be allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier.

Claims 1-35 are pending, however, claims 3, 11, 14-35 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to

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non-elected inventions, there being no allowable generic or linking claim. Claims 1, 2, 4-10, 12, 13 are under current examination.

Specification

The abstract of the disclosure is objected to because it should be in a separate sheet, the cover sheet of a WO publication is no longer acceptable as the abstract. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4, 5, 9, 10, 13 are rejected under 35 U.S.C. 102(e) as being anticipated by *Fischetti et al* (US 6,737,521).

Fischetti et al teach a composition comprising a live commensal oral organism such as *Streptococcus gordonii* (column 7, line 59), which is transformed by a plasmid vector expressing an antigenic polypeptide from a pathogen, such as *Bordetella pertussis* (column 7, line 12). *Fischetti et al* also teach the composition further

comprises the complete Freund's adjuvant (column 9, lines 16-20). Accordingly, *Fischetti et al* anticipate instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Fischetti et al* (US 6,737,521) as applied to claims 1, 2, 4, 5, 9, 10, 13 above, and further in view of *Walker et al* (Infect Immunity 1992;60:4260-68) and *Suehara et al* (US 6,051,240).

The teaching of *Fischetti et al* has been discussed above, *Fischetti et al* do not teach specifically which antigenic polypeptide from the *Bordetella pertussis* could be used as an effective vaccine.

Walker et al supplemented *Fischetti et al* by establishing that it is well known in the art that the pertussis toxin, particularly the S1 subunit of Pertussis Toxin is an

effective immunogen for inducing protective immune response against *Bordetella Pertussis*. *Walker et al* express the S1 subunit in attenuated *Salmonella typhimurium*, (fig. 1), which include the N-terminal 178 aa, and using such induced specific mucosal and systemic immune response in mice via oral immunization (abstract).

Suehara et al supplemented *Fischetti et al* by establishing that it is well known in the art that the pertussis filamentous, hemagglutinin, pertactin, as well as fimbriae are all protective components in developing vaccine for *Bordetella Pertussis*, and when combined, they could efficiently improve the vaccine strength (e.g. abstract).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method as taught by *Fischetti et al* by simply transforming the *Streptococcus gordonii* with the plasmid encoding the S1 subunit of Pertussis Toxin as taught by *Walker et al* and/or combined with other protective components as taught by *Suehara* with a reasonable expectation of success. Given the success as taught by *Fischetti et al*, *Walker et al* and *Suehara*, the skilled would have had a reasonable success. Thus, the claimed invention as a whole was *prima facie* obvious.

Claims 1, 2, 4-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Oggioni et al* (Vaccine 1995;13:775-9, IDS/A2) in view of *Walker et al* (Infect Immunity 1992;60:4260-68), and *Suehara et al* (US 6,051,240).

Oggioni et al teach a genetically modified live recombinant commensal *streptococci* expressing M6 protein of streptococcus pyrogens, E7 protein of human

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papillomavirus type 16 fused with M6 protein (see title and abstract), they teach "NON-PATHOGENIC GRAM-POSITIVE BACTERIA CAPABLE OF COLONIZING MUCOSAL SURFACES CAN BE ENGINEERED TO EXPRESS HETEROLOGOUS IMMUNOGENS. THESE RECOMBINANT STRAINS CAN OCCUPY A NICHE IN THE HOST'S MICROBIAL ECOSYSTEM, AND STIMULATE THE IMMUNE RESPONSE. THE STRAIN "CHALLIS" OF *STREPTOCOCCUS GORDONII*, ISOLATED FROM THE HUMAN ORAL CAVITY AND NATURALLY COMPETENT FOR GENETIC TRANSFORMATION, IS OUR MODEL HOST FOR EXPRESSION OF HETEROLOGOUS ANTIGENS (1st paragraph of the article)" *Oggioni et al* teach to inoculate the live recombinant vaccine vectors orally and intranasally (3rd paragraph of page 776), and induced a protective antibody response (see figures 1-3). *Oggioni et al* go on to teach that the live bacteria is advantageous in developing vaccine over killed bacteria because the later do not induce a systemic immune response (last paragraph). The teaching of *Oggioni et al* differs from the instant invention in that it does not particularly teach the Pertussis Toxin S1 subunit or other protective immunogens of *Bordetella Pertussis*.

Walker et al supplemented *Oggioni et al* by establishing that it is well known in the art that the S1 subunit of Pertussis Toxin is an effective immunogen for inducing protective immune response against *Bordetella Pertussis*. *Walker et al* express the S1 subunit in attenuated *Salmonella typhimurium*, (fig. 1), which include the N-terminal 178 aa, and using such induced specific mucosal and systemic immune response in mice via oral immunization (abstract).

Suehara et al supplemented *Oggioni et al* by establishing that it is well known in the art that the pertussis filamentous, hemagglutinin, pertactin, and fimbriae are all

protective components in developing vaccine for *Bordetella Pertussis*, and when combined, they could efficiently improve the vaccine strength (e.g. abstract).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by *Oggini et al* by simply substituting the M6 protein or fusion protein with an antigen protein of interest such as the S1 subunit of Pertussis Toxin as taught by *Walker et al* and/or other protective immunogens as taught by *Suehara et al* with a reasonable expectation of success. Given the success as taught by *Walker et al*, *Suehara et al*, and *Oggini et al*, the skilled would have had a reasonable success. Thus, the claimed invention as a whole was *prima facie* obvious.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is

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complete as evidenced by drawings, or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, p 1 "Written Description" Requirement*; Federal Register/ Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

The claims are directed to a composition comprising a live commensal oral organism genetically modified to express a plurality of immunogenic fragments and further express at least one mucosal adjuvant. However, the specification fails to disclose what protein compound is considered as mucosal adjuvant suitable for expressing by a commensal oral organism, and is able to enhance the immune response to the bacteria infection, and thus it fails to provide an adequate disclosure for claimed subject matter.

An adequate written description for an active agent requires more than a mere statement that it is part of the invention; what is required is a description of the chemical structures and physical properties itself. It is not sufficient to define the adjuvant solely by its principal biological property, i.e. "mucosal adjuvant", because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any agent with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all agents that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d

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1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). The court has made it very clear "CONCEPTION OF CHEMICAL COMPOUND REQUIRES THAT INVENTOR BE ABLE TO DEFINE COMPOUND SO AS TO DISTINGUISH IT FROM OTHER MATERIALS, AND TO DESCRIBE HOW TO OBTAIN IT, RATHER THAN SIMPLY DEFINING IT SOLELY BY ITS PRINCIPAL BIOLOGICAL ACTIVITY". *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

Since a skilled artisan does not know what agent is considered by the applicants as the mucosal adjuvant and suitable for expression by a genetic vector, one would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention. Therefore, the specification fails to meet the written description provision of 35 U.S.C. §112, first paragraph.

To the extent that the claimed invention is not described in the instant disclosure, claims 1 and 12 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described, and that is not conventional in the art.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730.

The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

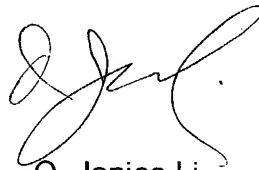
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It

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also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

A handwritten signature in black ink, appearing to read 'Q. Janice Li', with a stylized, flowing script.

Q. Janice Li
Primary Examiner
Art Unit 1632

QJL
December 23, 2004